LIVER STEATOSIS QUANTIFICATION USING MRI: A PROSPECTIVE COMPARATIVE STUDY WITH LIVER BIOPSY

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Introduction

Fatty infiltration of the liver is a common indicator of hepatocellular damage secondary to a variety of aetiologies. Pathogenesis of non-alcoholic fatty liver disease (NAFLD) is multifactorial, in the context of the so-called metabolic syndrome [1], combining obesity, diabetes, hypertension and hypertriglyceridemia [2], and associated with insulin resistance. In the United States, approximately 47 million individuals are estimated to have a metabolic syndrome [3]. The diagnosis of steatosis does have important therapeutic implications, because active management of obesity and a reduction in steatosis may improve liver injury and decrease the progression of fibrosis. The purpose of the present study was therefore to determine the accuracy of MR imaging in the assessment of the degree of liver steatosis, as compared with histological evaluation.

Method

This was a prospective single-institution study, approved by the Human Research Committee of our institution. Forty patients (20 women and 20 men; mean age 52.5 years old; range 23-78 years) with suspicion of chronic liver disease were referred for liver biopsy between April 2004 and February 2006.

MR imaging technique

MR imaging was always performed the same day before liver biopsy to avoid post biopsy artefacts. MR imaging was performed with a 1.5-T superconducting magnet (Magnetom Symphony, Siemens Medical Solutions, Erlangen, Germany). Imaging of the entire liver was performed by using a phased-array body coil. Each patient underwent a transverse T1-weighted in-phase (IP) and out-of-phase (OP) breath hold (22 seconds) spoiled gradient-echo sequence with a repetition time of 181 ms and an echo time of 2.38 ms for OP images and 4.76 ms for IP images; acquired with flip angles of 70°; slice thickness, 6 mm; slice gap, 0 mm; matrix 110 x 256; field of view 400 mm² and phase FOV 62.5%.

One blinded radiologist (NM) for clinical examination and pathological results interpreted all of the MR examinations and placed the ROI measurements on a picture and archiving workstation system (Impax; Agfa, Mortsel, Belgium). Fat/water ratio was calculated with the following formula SIout /SIin, were SIout is out-of-phase signal intensity and SIin is in-phase signal intensity [4].

Histopathology

Liver biopsies were performed by percutaneous sampling at variable segments in the right hepatic lobe with a 14-gauge needle. Tissue samples were fixed in buffered formalin and embedded in paraffin. Sections, 4 µm thick, were stained with hematoxylin-eosin-saffron, iron stain, and Masson trichrome reagents and evaluated by one pathologist. The histopathological evaluation was performed masked from any clinical information.

Steatosis was reported as the semi-quantitative evaluation of the percentage of hepatocytes (mild, moderate and severe) containing macrovesicular fat (fat droplet equal to or larger than the size of the nucleus, often displacing the nucleus) or microvesicular fat (numerous small fat droplets surrounding a centrally located nucleus). Its distribution within the lobule (zone 3 predominant, zone 1 predominant, panlobulmor, azonal) was noted.

Statistical analysis

Fat/water ratio was correlated with the pathologic degree of steatosis by using a linear regression analysis and Pearson correlation coefficient (r) (XL stat-pro for excel, Addinsoft, Paris-France). The threshold value in Fat/Water ratio used to distinguish between no steatosis and hepatic steatosis is the most significant decision in the area of clinical diagnosis. ROC (receiver operating characteristic) curves are a useful tool to facilitate taking this decision. The overall diagnostic performance of the pathological grading in the diagnosis of 20% or higher liver steatosis was compared with that of Fat/Water Ratio by ROC analysis.

Results

The final diagnosis in the patients of the study group was: NAFLD in 18 patients, alcoholic steatohepatitis in 9 patients, cholangiopathy in 3 patients, autoimmune hepatitis in 4 patients, other in 6. Histological analysis disclosed that liver steatosis was present in 82.5 % of cases (n=33). Fatty infiltration of the liver was mild (<30%) in 18 patients, moderate (30-60%) in 10 patients and severe (>60%) in 12 patients. The mean percentage of steatosis was 39 ± 29.2 % (range 0 to 90%). Macrovesicular steatosis was present in 79% of cases (n=26), microvesicular steatosis in 6% (n=2), and association of macrovesicular and microvesicular steatosis in 15% of cases (n=5). Thirty-six patients presented with liver fibrosis: F1 in 17 patients (42.5%), F2 in 9 patients (22.5%), F3 in 4 patients (10%) and F4 in 6 patients (15%). 50% of NAFLD patients (n=10) had a NAS score ≥ 5 and were therefore considered to have NASH (Figure 1).

MR imaging results

The mean ratio of signal intensity between T1-weighted out and in phase image was 0.7 ± 0.31. This ratio was statistically different between patients with liver fatty infiltration (fat/water ratio = 0.63 ± 0.28) and patients without steatosis (fat/water ratio = 1.07 ± 0.15). The fat/water ratio had a positive correlation with steatosis grade on liver biopsy ($p < 0.0001$), the coefficient of linear regression corresponding to r = 0.798 (Figure 2). The relation between the histological grade of steatosis and the fat/water ratio can therefore be expressed by the following formula: %Steatosis = [(-79.8)*(Fat/Water ratio)] + 91.5.

Fat/Water ratio (cutoff value ≥ at .93) revealed liver steatosis defined by the presence of equal or more 20 % of intracellular lipids with a sensitivity of 93 % and a specificity of 86 %.

	All patients		NAFLD patients		Other pathology	
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD
Steatosis (%)	33	39 ± 29 %	18	45 ± 28 %	15	29 ± 25 %
Fibrosis stage	37	1,94 ± 1,17	18	2,17 ± 1,1	18	1,8 ± 1,19

Figure 1: Results of histological examination

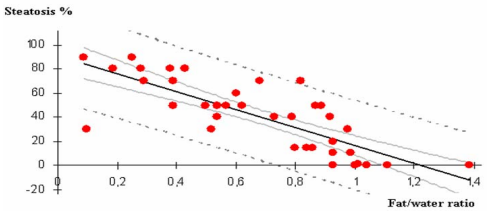

Figure 2: Relation between histological fatty liver infiltration and fat/water ratio. For fatty infiltration of more than 20%, the sensibility and the specificity of MR fat quantification were 96% and 93% according to ROC curve, respectively.

Conclusion

Our study strongly suggests that comparison of T1-weighted gradient echo in-phase and out of phase images is an efficient method for the diagnosis and quantification of liver steatosis with only one short TR series.

References

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